out non-specific cell activation by anticellular antibodies. The same sera also enhanced HIV_{SF33}-induced plaque formation in the MT4 T cell line[3] at titres up to 50 (table I). The control normal sera or corresponding pre-bleed of the animals did not show any effect. Addition of fresh unheated normal guineapig serum did not alter the results. HIV_{SF2} and HIV_{SF128A} are blood and brain isolates from AIDS patients, respectively. HIV_{SF2} was used to infect the chimpanzee and HIV_{SF128} for immunisation of the guineapig. Neither isolate productively infects MT4 cells, and the animal enhancing sera did not change this property. However, HIV_{SF2}, a non-macrophage-replicating isolate,[4] was able to grow in primary monocytes/macrophages in the presence of minimally diluted enhancing serum (table I). Preadsorption of the guineapig serum by 'Sepharose CL4B-protein A' removed its enhancing activity and the eluates from this resin restored the activity (data not shown).

Heat-inactivated sera from three HIV seropositive individuals also enhanced the infectivity of HIV, although the effects seemed to be more restricted (table II). Only HIV_{SF170}, an African isolate,[2] was consistently enhanced by all three sera, whereas HIV_{SF2} or HIV_{SF128A} were enhanced by one serum only. The US serum neutralised the two American HIV strains but enhanced infection by the African isolate. Addition of fresh unheated human or guineapig serum did not affect the enhancing titres. As with the animal sera, this result contrasts with those of Robinson et al. Two reasons may account for this difference. First, our sera were selected for their enhancing activity despite heat inactivation, whereas Robinson et al mainly studied the effect of complement on neutralising sera. Second, we defined enchancement as amplification of productive viral infection; this is distinct from syncytia formation and cytopathic effects measured in the other study. Our data thus point to a second mechanism responsible for antibody-dependent enhancement of HIV infectivity in vitro. This mechanism is not affected by heat treatment, prolonged storage at 4°C, repeated freeze/thaw of the sera, or addition of fresh untreated serum to the reaction mixture; it therefore seems to be independent of the presence of complement. The removal and restoration of enhancement by preadsorption of the guineapig serum with protein A suggest that the enhancing factor is an immunoglobulin. One possible mechanism of complement-independent enhancement could be the attachment and internalisation via Fc receptors of virus-antibody complexes in macrophages[5] or T cells. Activated T cells as well as macrophages have been reported to express one or more of three defined Fc receptors depending on the stage of differentiation and activation of these cells.[6,7] Alternatively, another as yet unidentified receptor on T cells and macrophages or a receptor-independent mechanism could be involved.

The production of enhancing factors to HIV in immunised animals raises serious concern about the types of antibodies that could be elicited by vaccine approaches in man. Our preliminary observations indicate that some isolates are more susceptible to enhancement than others. Such viruses could prove valuable for identifying the epitope(s) responsible for antibody-dependent enhancement that should be removed from vaccine preparations.

Supported by a grant from the National Institutes of Health (RO1-AI-24499).

Cancer Research Institute,
University of California,
San Francisco, California 94143, USA

JACQUES HOMSY
MASATOSHI TATENO
JAY A. LEVY

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WHAT IS MYALGIC ENCEPHALOMYELITIS?

SIR,—To improve our knowledge of the pathophysiology of myalgic encephalomyelitis (ME), it is essential that only one name is used to describe the disorder and that reproducible diagnostic criteria are agreed. Having reviewed the clinical and laboratory features of over 200 patients with well characterised ME, we agree with the Centers for Disease Control (CDC)[1] that the best term is the chronic fatigue syndrome (CFS). We have developed and evaluated a set of diagnostic criteria after reviewing 100 patients with CFS diagnosed by a characteristic history (especially muscle fatigue), a normal physical examination (excluding the findings of lymphadenopathy, muscle tenderness, or pharyngitis), and negative investigations to exclude other chronic infectious or immunoimpairing diseases.

The prevalence of the various symptoms and signs was used to define the following criteria for a diagnosis of CFS: (1) generalised, chronic persisting or relapsing fatigue, exacerbated by very minor exercise, causing significant disruption of usual daily activities, and of over six months' duration; and (2) neuropsychiatric dysfunction including impairment of concentration (difficulty in completing mental tasks that were easily accomplished before onset of syndrome) and/or onset of short-term memory impairment; and/or (3) abnormal cell-mediated immunity indicated by reduction in absolute count of T8 and/or T4 lymphocyte subsets, and/or cutaneous anergy. In addition, the following findings are supportive: myalgia, arthralgia, headaches, depression, tinnitus, paraesthesiae, and sleep disturbance persistent over six months with no other cause, and lymphadenopathy, localised muscle tenderness, and pharyngitis (on two or more occasions after the initial illness).

Abnormal cell-mediated immunity has been reported in patients with CFS,[2] including T-cell lymphopenia and reduced T-cell function in vitro measured by a phytohaemagglutinin (PHA) stimulation assay. We have confirmed such abnormalities in a controlled study in which absolute T-cell subset counts and T-cell function measured in vitro by PHA stimulation assay were abnormal in 81 of 100 patients (unpublished). The proposed diagnostic criteria therefore incorporate these immunological abnormalities.

A further 100 patients defined by our criteria have been followed up for at least 12 months. In only 2 patients was a possible alternative diagnosis reached—endogenous depression in 1 case and chronic active hepatitis (probable non-A, non-B) in the other.

The CDC criteria require or recommend the exclusion of over thirty diseases by at least twenty laboratory investigations, before the complex clinical criteria may be even considered. Our criteria highlight the central positive features of the syndrome, supported where appropriate by laboratory investigations. Patients with CFS may well be heterogeneous, but we believe our criteria will define most of this population and that their disorder will have a common pathogenesis.

Other names for CFS have included post-viral syndrome or post-viral fatigue syndrome, because symptoms often follow an illness suggestive of viral infection.[3] In America, chronic Epstein-Barr virus (EBV) infection has been thought to be the basis of most cases of CFS.[4] However, many such cases were labelled after the demonstration of high titres of IgG anti-EBV antibodies, now shown to be of uncertain significance.[3,4] Infections other than viruses may precipitate CFS. We have found that *Toxoplasma gondii* and *Brucella abortus* can produce an identical syndrome, after a serologically confirmed initial illness. Therefore post-viral syndrome is an inappropriate name. Even post-infection fatigue syndrome is not appropriate since many patients with CFS have an insidious onset of illness without a defined initiating infection. We have seen several cases in which vaccination (against tetanus, cholera, influenza, or typhoid) was associated with onset of the syndrome without coincident infection, which suggests that antigenic challenge, not necessarily in the form of an infection, may be the prerequisite for the development of the disorder.

ME is the most inappropriate name of all. Myalgia is not universal among patients with the syndrome and there is usually no laboratory evidence of encephalitis or myelitis. In addition, the name ME has a connotation of hysterical illness, which is clearly

invalid in the face of evidence of persistent infection[5] and immunological dysfunction.[2,6,7] CFS is therfore the most appropriate name,[1] at least until the pathophysiology is defined.

A. R. LLOYD
D. WAKEFIELD
C. BOUGHTON
J. DWYER

The Prince Henry Hospital and Schools of Pathology and Medicine, University of New South Wales, Sydney, Australia

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DOPPLER UTEROPLACENTAL WAVEFORMS

SIR,—Whilst we agree with Dr Hanretty and colleagues (April 16, p 850) that caution is required before allowing doppler waveforms obtained from the uteroplacental circulation to affect management critically, we disagree with many aspects of their study. Here we confine ourselves to two criticisms.

The initial work[1] in this field was done with duplex, pulsed doppler equipment which, in most cases, allowed simultaneous imaging of the vessel under study. When a uteroplacental vessel could not be visualised the internal iliac artery was located and the myometrium superolateral to that artery was searched until a characteristic waveform was obtained. Knowledge of the position of the range gate of the duplex equipment allowed us to ensure that signals were not collected from a vessel in the anterior abdominal wall. Using such equipment we have reported reference ranges for the commonly used indices from both the fetal and the uteroplacental circulation.[2]

Experience with such equipment showed that each vessel produces a characteristic waveform, both in health and in disease. This is complicated in the uteroplacental circulation because the signal from an internal iliac artery closely resembles that of a high-resistance pattern obtained from a uteroplacental vessel (fig 1). Hanretty et al's fig 2 demonstrates an internal iliac artery in the upper channel and not, as they suggest, a high-resistance pattern from a uteroplacental vessel. As the pulsatility index from the internal iliac artery is higher than that obtained from a healthy uteroplacental vessel this error would be expected to elevate falsely the range for the control group, which could explain why Hanretty

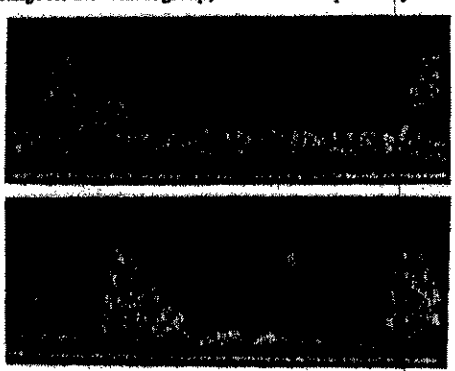

Fig 1—Waveforms from uteroplacental artery demonstrating high-resistance pattern (upper) and from internal iliac artery (lower).

Both waveforms obtained by duplex, pulsed doppler equipment with the vessel clearly visualised.

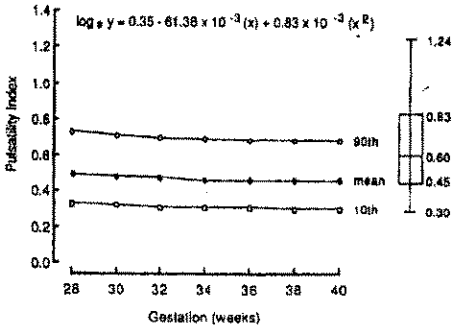

Fig 2—Reference range from pulsed doppler equipment.[2]

Box-whisker plot illustrates median and quartiles extrapolated from Hanretty et al's fig 1; their control group is skewed towards higher values.

and colleagues fail to demonstrate a difference between their controls and the groups with pregnancy induced hypertension. Support is lent to this contention by comparing the results from their controls with our reference range (fig 2).

We find it difficult to follow Hanretty et al's logic in choosing the waveform that represents the lowest vascular resistance. Schulman et al,[3] using waveform patterns obtained from the left and the right sides of the uterus, classified waveforms as all normal in 40 patients, all abnormal in 13, or divergent in 18. They demonstrated a "dose-dependent" effect in that the incidence of pregnancy induced hypertension increased from 14% to 33% to 73% in their three groups, respectively. This suggests that the most abnormal waveform (usually from the non-placental side of the uterus) should be used to classify patients with hypertension. The prediction of pregnancy outcome from waveforms obtained in early pregnancy is most sensitive when based upon the worst waveform.[4,5]

The introduction of colour-flow doppler, whilst expensive, will allow precise localisation of the appropriate vessel and should therefore remove the error of inexperience.

Department of Obstetrics and Gynaecology, St George's Hospital Medical School, London SW17 0RE

J. MALCOLM PEARCE
PETER MCPARLAND

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SIR,—We agree with Dr Hanretty and colleagues that controlled studies of doppler ultrasound in the evaluation of pregnancy-induced hypertension (PIH) are needed. However, their study leaves many questions unanswered.

Our main criticism rests in their selection of the lowest pulsatility index (PI) at an unspecified location in the uterine wall as the predictor of abnormality. We have always taken signals from uterine vessels medial to the external iliac artery and, using colour flow mapping,[1] we have found that the vessels we originally[2] "believed" to be arcuate arteries are in fact the main uterine artery or major branches of that vessel. Our normal ranges are slightly higher than those of Schulman et al[3] who obtained signals from near the origin of the vessel, and this is our current practice. We have also found that the best predictor of PIH and intra-uterine growth retardation are the non-placental uterine vessels because "being part of a continuous arcade, the non-placental artery reflects a summation of all placental bed and myometrial arteries".[4] These observations are in agreement with Fleischer et al.[5]